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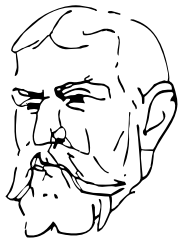

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CASE STUDIES

CASE STUDY

A CASE OF KAWASAKI DISEASE IN AN EIGHT-YEAR-OLD BOY

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Ganna K. Kopiyka[1], Tetiana Y. Kravchenko[1], Olena M. Artomova[2], Krystyna B. Soboleva[1]
[1]ODESA NATIONAL MEDICAL UNIVERSITY, ODESA, UKRAINE
[2] COMMUNAL NON-PROFIT ENTERPRISE «CHILDREN'S CITY CLINICAL HOSPITAL №3» OF THE ODESA CITY COUNCIL, ODESA, UKRAINE

ABSTRACT

Kawasaki disease is an acute systemic disease characterized by the predominant lesions of middle and small arteries, alongside destructive and proliferative vasculitis development. The aetiology is currently being discussed. Infectious factors are mostly preferred, in addition, autoimmune mechanisms and genetic heredity are considered. The diagnosis of Kawasaki disease is established by clinical signs; laboratory changes are usually taken into account as are ancillary criteria.

The article discusses the clinical case of Kawasaki disease in an 8-year-old boy. Given the variety and inconsistency of the clinical symptoms (the child had four of the five mandatory criteria together with prolonged fever), there was a late diagnosis, namely on day 10 of the disease.

Due to the high risk of cardiovascular complications in the differential diagnosis of children with fever lasting more than 3 days should be considered Kawasaki disease, followed by mandatory heart echocardiography during the first 10 days of the disease, especially if the fever is accompanied by the increase of acute phase reactants. When treating children with chronic fever without a specific source, the doctor should be wary of Kawasaki disease, as it can clinically simulate acute respiratory viral disease, the onset of diffuse connective tissue disease, and infectious endocarditis, and can have common features and require differential diagnostics with coronavirus associated multisystem inflammatory syndrome.

KEY WORDS: mucocutaneous lymph node syndrome, vasculitis, paediatrics

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INTRODUCTION

Kawasaki disease (KD), or mucocutaneous lymph node syndrome, is an acute systemic disease characterized by the predominant middle and small arteries lesion and the destructive proliferative vasculitis development. It is usually a self-limiting condition in which fever and inflammation last for about two weeks without treatment. However, KD can cause aneurysms and coronary artery stenosis. Thus, KD is one of the causes of acquired cardiovascular disease. The aetiology of the KD is currently being discussed. Most authors consider the infectious factor to be the most significant (mostly viral), which explains the peak incidence in spring and winter [1]. In addition, autoimmune mechanisms and genetic heredity are considered as factors in the development of KD. There are 11 known genetic loci associated with this disease [2]. KD is more common in Asia, where it was first described by T. Kawasaki in 1967. Thus, KD in Japan occurs with a frequency of 330 cases per 100,000 children. In contrast, in North America, Australia and Europe, there are only 19,7 to 29,8 cases per 100,000 children [3]. Children under 5 years get sick more often, but the disease is also registered in older children. It should be noted that all statistics on KD are usually understated due to significant difficulties in diagnosis and the exceeding presence of incomplete disease forms.

Attention to KD has recently increased significantly due to the COVID-19 pandemic. Some similarities between the immune response in multisystemic inflammatory syndrome in children, which occurs in the body in response to coronavirus, and the changes that are characteristic of KD complicate diagnostics [1,4,5].

KD is a clinical diagnosis, which means that there are no specific laboratory tests to confirm the diagnosis. Laboratory changes are usually considered as supportive criteria[6]. Thus, classic KD is characterized by: fever lasting more than 5 days without any other explanation, and the presence of at least 4 of the following 5 criteria: bilateral conjunctival injection; changes in the oral mucosa (redness and cracks of the lips, injection of the pharynx, or strawberry tongue); changes in the peripheral extremities (erythema of the palms and/or feet, swelling of the hands or feet – in the acute phase and desquamation – in the recovery phase); polymorphic rash (maculopapular or scarlet fever-like rash involving the extremities, torso, perineum); cervical lymphadenopathy (at least 1 lymph node ≥1.5 cm in diameter) [6].

The oral mucosa lesions are observed in approximately 90% of KD cases, polymorphic rash in – 70-90%, changes in the extremities – in 50-85%, ocular changes – in 75% and cervical lymphadenopathy – in 25-70%[4]. A significant difficulty in the diagnosis is that the KD manifestations do not occur simultaneously, but sequentially and do not have a typical occurrence order, making it difficult to combine separate symptoms into an overall picture of the disease. The number of incomplete disease forms is also increasing, in which in addition to fever there are not 4, but only 2-3 symptoms [7].

Brief description of the main manifestations. Fever is the most significant sign of this disease. It is pertinacious and resistant to antipyretics. The "diagnostic minimum" is 5 days, but it lasts much longer usually. The main symptoms tend to appear during the first 10 days amid fever. Conjunctivitis is always bilateral, non-exudative, and begins within a few days of the fever onset. Photophobia may occur. Mucositis often becomes apparent as KD progresses. There are cracked red lips and "strawberry tongue", which is the result of the filamentous papillae obstruction. The rash is often polymorphic, beginning within the first few days. Skin changes may also be manifested by redness or crusting at the Bacillus Calmette-Guérn vaccination site. Changes in extremities are the latest manifestation in the vast majority of cases. Swelling of hands and feet often occurs, as does diffuse of palms` and soles`. Noted can be leaf-like desquamation in the convalescence phase, which also begins with the arms and legs. As for lymphadenopathy, it is the least consistent sign of KD, which may be absent in half or even three-quarters of patients. Usually anterior cervical nodes are involved; one large node is often palpable, although ultrasound usually reveals numerous nodes located like a grape bunch [7-9].

Cardiovascular manifestations are not a part of the diagnostic criteria for KD, but they support the diagnosis. Gallop sounds and tachycardia may be observed during the first 10 days, which is proportional to the fever severity. These symptoms are the result of lymphocytic myocarditis, which usually occurs in KD. In addition, heart sounds may be muffled due to pericardial effusion, which occurs in approximately 30% of patients, but is usually small in volume. Among all the cardiovascular system manifestations the most dangerous ones are myocarditis, heart failure and coronary artery aneurysms, which usually develop within the first 7 to 10 days after the onset of the disease. The latter makes early diagnosis and treatment relevant. Therefore, echocardiography should be performed in all patients with KD as soon as there are suspicions of the diagnosis so that a benchmark for further monitoring of the dynamics and evaluation of the effectiveness of treatment could be set [10-12].

Arthritis is also not a diagnostic criterion, but it occurs in almost 25% of patients with KD. Large joints (knees, ankles and hips) are the first to be involved. Arthritis is usually limited and does not deform the joints [7-9].

Other manifestations, such as diarrhoea, vomiting, abdominal pain, cough, rhinorrhoea, and irritability prevail in the prodromal period [13]. Tonsillitis, pneumonia symptoms or urinary tract infections are also common at the onset of the disease. However, the persistence of fever after the antibiotic's treatment raises doubts about the diagnosis and gives reason to continue the diagnostic search.

Laboratory evaluation. Although laboratory criteria are not included in the classic diagnostic criteria, they can nevertheless support the diagnosis of KD in ambiguous cases, so they are useful in diagnostic algorithms. Typical manifestations include acute phase reactants increase, such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR). Thrombocytosis usually develops after the seventh day of illness, leucocytosis and a left shift. Normochromic and normocytic anaemia are also common [7-9].

Intravenous immunoglobulin (IVIG) treatment during the first 10 days of illness reduces the coronary artery aneurysms incidence 5-fol compared to untreated children. Usually a single dose of IVIG is prescribed at the rate of 2 g/kg, which is administered within 8 to 12 hours. IVIG should be administered in cases of late diagnosis, even after 10 days, if the patient has signs of vasculitis or systemic inflammation (persistent fever, increase of the acute phase of inflammation). During the acute phase of the disease, it is also recommended to administer aspirin in a wide range of doses (30-100 mg/kg/day). The dose of aspirin should be reduced in 48 hours after fever cessation to 3-5 mg/kg/day and continued until laboratory inflammation signs (ESR, CRP, platelet count) return to normal, in the absence of coronary artery abnormalities according to echocardiography echocardiography [6,14,15].

CASE REPORT

An 8-year-old boy was hospitalized with complaints of prolonged fever up to 39°-39.5°C, skin rash on the torso, perineum and extremities, swelling of the hands and feet, general weakness, and catarrhal phenomena. Hospitalization took place on the 8th day of the disease; the child's general condition was assessed as moderately severe. After taking a medical history it was detected that the disease began acutely with a rise of body temperature to 39°C, which couldn't be lowered with antipyretics. During the first three days the temperature ranged from 39 to 39.5°C. Taking paracetamol and ibuprofen in doses appropriate to the age reduced the fever for a short interval of 2-3 hours by 0.5°C.

At the end of the 3rd day of the disease there were symptoms of bilateral catarrhal conjunctivitis, changes in the oral cavity – "strawberry tongue", throat hyperaemia, and chapped lips; this was accompanied by growing fatigue. The child was examined by a paediatrician on an outpatient visit; the situation was considered as manifestations of acute viral infection. The patient was prescribed symptomatic therapy: nasal lavage, throat lozenges and antipyretics.

On the 4th day, a rash appeared in the perineum area. Subsequently, the rash spread to the limbs and torso (Figure 1, 2).

The rash was scarlatiniform and was not accompanied by itching. When the rash appeared, the child was examined by an infectious disease physician who found no reliable data in favour of any specific infectious pathology.

The blood count was performed on the 5th day of disease and revealed leucocytosis up to $13x10^9$/L, increased ESR to 38 mm/h, and decreased haemoglobin to 109 g/l; the rest of the indicators were within normal limits. On the same day, after the doctor's examination, the mother made the decision to start antibacterial therapy with azithromycin by herself. In Ukraine, pharmacies are not forbidden to sell antibiotics without medical prescription. No outpatient

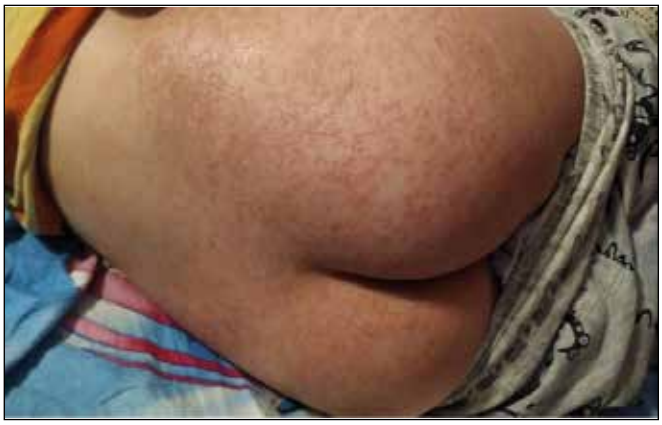

Fig. 1. Rash on the buttocks

Fig. 2. Rash around the elbow joint

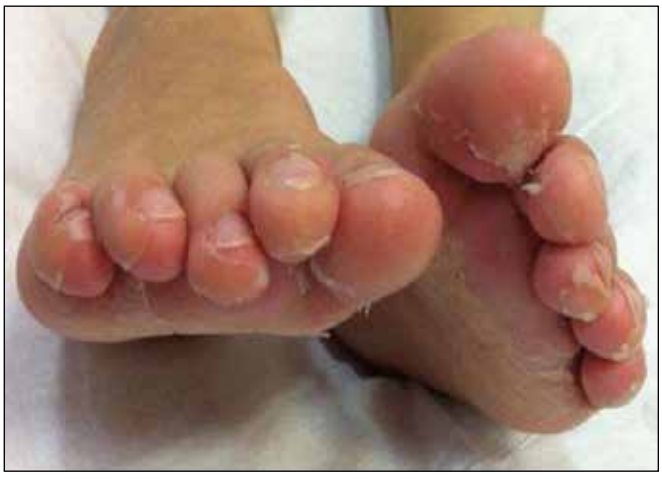

Fig. 3. Desquamation of the skin of the palms and sole

paediatric follow-up took place. The fever of 39°-39.5°C continued and the child was given antipyretics to relieve symptoms. No positive dynamics were observed during the disease.

Swelling of the extremities appeared on the 8th day after the disease onset. An ambulance was called and the child was admitted to the hospital. Blood count revealed: leucocytosis – $15x10^9$/L, increased ESR to 50 mm/h, thrombocytosis – $540x10^9$/L, increase in CRP – three times. After the hospital admission it was decided to start antibacterial therapy ex juvantibus, due to the increase in acute haematological parameters in the dynamics, duration of fever, prior inadequate antibacterial therapy and, consequently, the lack of response to it. Later a broad-spectrum antibiotic was prescribed from the 3rd generation cephalosporin group, namely ceftriaxone in the appropriate dosage according to the age and weight of the child. A diagnostic search was launched simultaneously with the start of therapy, which was aimed at identification of a possible infection source.

On the 9th day from the start of the disease (on the second hospitalisation day) the child developed pain in the knee joints without visual inflammation signs. Instrumental and laboratory data revealed the following: chest X-ray – without changes, blood culture for sterility, examination for typhoid-paratyphoid infection Taking into consideration the epidemiological situation was conducted an examination for COVID-19: PCR test (twice), IgM, IgG levels determination, which results were also negative, hence excluding both – the presence of atypical long-term coronavirus infection and the active stage of the disease (Differential diagnosis with multisystem inflammatory syndrome). Ultrasound examination of the abdominal cavity and joints did not reveal pathological changes. Tachycardia was found during auscultation, that correlated with the level of fever, the ECG revealed transient incomplete right bundle branch block. During the first two days of the child's hospital stay, the rash remained within the extremities, perineum and torso, there was no itching, the desquamation phenomenon increased over time (Figure 3).

Conjunctivitis and "strawberry tongue" regressed. The area of pain spread from the knees to the hips. The enlargement of peripheral lymph nodes was not observed during the entire period of the disease. Swelling of the extremities lasted for two days. After 48 hours of the ceftriaxone treatment, no response to antibacterial therapy was noted, the child continued to have a fever, and his general condition remained moderate.

From 10th of the disease, glucocorticosteroid therapy was prescribed at a dose of 2 mg/kg/day of prednisolone, which reduced joint pain and had a partial effect on fever level: the temperature dropped to subfebrile values and increased only twice a day. KD was suspected in a child after receiving the results of the abovementioned laboratory and instrumental studies and the analysis of the existing clinical symptoms (bilateral catarrhal conjunctivitis, changes in the oral mucosa in the form of cracked lips, redness, "strawberry tongue", changes in the extremities in the form of redness, swelling, and skin rash that was followed by desquamation) that were associated with prolonged fever.

Echocardioscopic transthoracic examination was performed on the 11th day of the onset. No ultrasound data in favour of coronary artery dilatation were detected. Thus, the child was diagnosed with KD due to the presence of 4 of the 5 mandatory criteria with the underlying prolonged fever.

Based on the fever regression on the 12th day from the disease onset and the absence of coronary artery disease, as

well as the stabilisation of the patient's general condition, intravenous immunoglobulin was not administered, the antibiotic was discontinued and aspirin was prescribed at 5mg/kg/day [6,14,15]. The child remained under observation in the hospital for another three days. There were observed improvements in general condition, body temperature normalisation, arthralgia, oedema of the extremities and skin rash regression, and the spread of desquamation. There was a positive trend in laboratory parameters: the total leukocytes count was $11x10^9$/L, total platelets count – $480x10^9$/L, ESR remained at 45 mm/h, CRP decreased by half. Biochemical parameters (kidney and liver tests, glucose, total protein levels) did not demonstrate abnormalities during the disease.

The child was discharged in good health with the following recommendations:

- To continue aspirin taking at a dose of 5 mg/kg/day until inflammatory markers stabilization;
- To monitor body temperature daily monitoring before taking aspirin;
- To perform echocardioscopy in 2 and 6 weeks under the cardiorheumatologist`s supervision.

We present a clinical case of KD in an 8-year-old child. The peculiarity of this case was the late diagnosis on the 11th day from the disease onset. Late diagnosis can be explained by the gradual onset of clinical symptoms, lack of adequate dynamic monitoring of the child's condition at the outpatient stage and delayed child`s hospitalization in the hospital. The clinical picture was characteristic of the full form of the KD and contained 4 of 5 mandatory symptoms together with prolonged fever: bilateral catarrhal conjunctivitis, changes in the oral mucosa in the form of chapped lips, redness and "strawberry tongue", changes in the extremities (in the form of hyperaemia and oedema, scarlatiniform rash followed by desquamation). Of the accessory symptoms, the child had arthralgias which is not of diagnostic value but may support the diagnosis. In this case, the disease was moderate and no cardiovascular complications were observed. IVIG was not administered due to diagnosis later than 10 days, no coronary artery disease, and regression of fever at the time of diagnosis. For prophylactic purposes, aspirin was prescribed and further monitoring of the echocardioscopic picture of the heart and coronary vessels was recommended [6,14,15].

CONCLUSIONS

1. There are significant difficulties in the early diagnosis of KD due to the variety and gradual symptoms onset, the lack of definitive diagnostic tests, the course of the disease in the form of atypical or incomplete forms.
2. Due to the high risk of cardiovascular complications, the diagnosis of KD should be considered in the differential diagnosis in children with fever lasting more than 5 days with mandatory echocardioscopy performed during the first ten days of the disease, especially if fever is accompanied by an increase in acute phase reactants.
3. Children who have KD need further careful cardiovascular system monitoring.
4. Paediatricians and family physicians should be suspicious about KD, because it can have a similar course to the acute respiratory disease, with the diffuse onset of connective tissue disease, infectious endocarditis, and have common features with multisystemic inflammatory syndrome in children with COVID-19 which determines the need for differential diagnosis.

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ORCID and contributionship:
Ganna K. Kopiyka: 0000-0002-1378-0195 [A,D,F]
Olena M. Artomova: 0000-0001-7720-0498 [A,B]
Tetiana Y. Kravchenko: 0000-0002-2700-8323 [B,D,E]
Krystyna B. Soboleva: 0000-0003-06358030 [B]

Conflict of interest
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Ganna K. Kopiyka
Odesa National Medical University
2 Valikhovsky st., 65000 Odesa, Ukraine
tel: +380963374882
e-mail: ann_29@ukr.net

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